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# Effects on cardiopulmonary parameters of propofol, Ketofol and Etomidate as induction agent in glycopyrrolate premedicated dogs maintained under isoflurane anaesthesia

**Rahul Paul, Basanta Saikia, Hitesh Bayan, Bedanga Konwar, Analisha Debbarma and Chang L**

**Abstract**
The present study was undertaken in 18 dogs with elective surgery (castration, spaying etc.) to evaluate the effect of propofol, ketofol and etomidate as induction agents in glycopyrrolate premedicated dogs maintained with isoflurane. The animals were randomly divided into three groups *viz*. group P, KP & E, comprising six animals in each group. All the animals of the three groups were premedicated with glycopyrrolate @ 0.01 mg/kg IM, 10 minutes prior induction. Propofol @ 6mg/kg IV, ketofol @ 4mg/kg and etomidate @ 3mg/kg was administered as induction agent in group P, KP and E respectively. Maintenance of anaesthesia was carried out by using isoflurane in all the animals. Cardiopulmonary parameters were studied at (baseline) 0 min and thereafter 5, 15, 30, and 60 minutes after induction. Heart rate significantly ($P< 0.01$) increased in all the groups compared to baseline at 5 min time interval and then gradually decreased towards the baseline. Respiration rate significantly ($P< 0.01$) decreased in group KP but non significantly in group P and E. Rectal temperature significantly ($P< 0.01$) decreased in group P and KP but non significantly decreased in group E. Significant ($P< 0.05$) decrease in SpO2 was observed in group P whereas significant ($P< 0.01$) decrease in SpO2 was observed in group KP and E followed by gradual increase in SpO2 in all three groups Non significant increase in ETCO2 followed by gradual decrease towards the baseline was observed in all three groups. Significant ($P< 0.01$) decrease in SP and DP was observed in group P whereas significant ($P< 0.01$) increase in SP and DP was observed in group KP. In group E non significant changes were observed in group E.

**Keywords:** Propofol, Ketofol, Etomidate, glycopyrrolate and induction agent

## Introduction
Propofol (2, 6-diisopropyl phenol) is an injectable anaesthetic agent belonging to the alkyl phenol group, a rapid onset of action, short duration of action with a complete and excitement-free rapid recovery, with good muscle relaxation, but with poor analgesic properties (Zoran *et al.*, 1993, and Hall *et al.*, 2001) [5]. Ketofol administration offered effective sedation for spinal anaesthesia for gynaecologic, ophthalmologic and cardiovascular procedures in all age groups. The main advantage of this drug combination over alone propofol administration is the opposing hemodynamic and respiratory effects of each drug that enhance safety and efficacy and decrease the dose of propofol required for induction (Daabiss *et al.*, 2009) [4]. Etomidate is a carboxylate imidazole derivative nonbarbiturate, short-acting, IV anaesthetic. Etomidate is characterized by better hemodynamic stability, minimal respiratory depression, and cerebral protective effects (Robert and Hiller, 2006) [12]. The present study was undertaken to evaluate Effects of propofol, Ketofol and Etomidate on cardiopulmonary parameters as induction agent in glycopyrrolate premedicated dogs maintained under isoflurane anaesthesia.

## Materials and Methods
The animals were randomly divided into three groups *viz*. group P, KP & E, comprising six animals in each group. All the animals of the three groups were premedicated with glycopyrrolate @ 0.01 mg/kg IM, 10 minutes prior induction. Propofol @ 6mg/kg IV, Ketofol @ 4mg/kg and etomidate @ 3mg/kg was administered as induction agent in group P, KP and E respectively. Maintenance of anaesthesia was carried out by using isoflurane in all the animals in all three groups.

Heart rate, respiratory rate, rectal temperature, SpO2, ETCO2 and NIBP were studied at (baseline) 0 min and thereafter 5, 15, 30, and 60 minutes after induction. Statistical analysis was carried out by SPSS version 20.

**Results and discussion: Heart rate (beats/min)**

The heart rate in all three groups increased significantly ($P< 0.01$) after 5 minutes compared to baseline and thereafter it decreased gradually till the end of observation in both group P and KP whereas in group E it remains almost constant till the end of study period after initial increase.

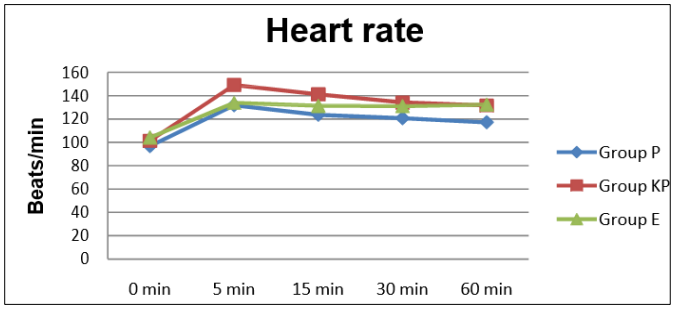


**Fig 1:** Heart rate (beats/min) at different time intervals in groups P, KP and E

Heart rate increased at 5 min after induction might be due to administration of glycopyrrolate in all three groups as glycopyrrolate (or other anticholinergics drug) caused increase heart rate Jacobson *et al.* (1994) [7], Shinde *et al.* (2018) [16] and Saikia *et al.* (2019) [14]. In both group P and KP after initial increase gradual decrease in heart rate was observed throughout the study period due to effect of propofol Brussel (1989), Amengual *et al.* (2013) [1], Thejasree *et al.* (2018) [18], Shinde *et al.* (2018) [16] although in group KP at 5 min heart rate was significantly ($P< 0.01$) higher from other two groups and then gradual decrease in heart rate was observed throughout the study period similar findings were observed by Shinde *et al.* (2018) [16], Thejasree *et al.* (2018) [18] and Saikia *et al.* (2019) [14]. In group E significant increase in heart rate was observed up to 5 min and thereafter non significant changes throughout the study period Sams *et al.* (2008) [15] and Rodriguez *et al.* (2012) [13]. Cardiovascular stability with etomidate might be due to no effect of etomidate in baroreceptor function and sympathetic nervous function after its administration.

**Respiratory rate (breaths/min)**

The mean values of respiratory rate recorded in different periods of observation did not show any significant difference ($P>0.05$) in the group P and E although non significant decrease in respiration rate was observed up to 15 min then gradual increase towards the baseline was observed with propofol and with etomidate by Sams *et al.* (2008) [15], Rodriguez *et al.* (2012) [13], Shinde *et al.* (2018) [16], Thejasree *et al.* (2018) [18] and Saikia *et al.* (2019) [14].

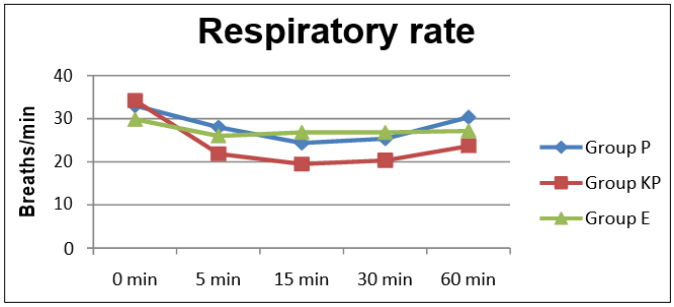


**Fig 2:** Respiratory rate (breaths/min) at different time intervals in group P, KP and E

The respiratory rate was significantly decreased in group KP during anaesthetic trial with maximum decrease at 15 min time interval than gradual increase in respiration rate towards the baseline was observed similar findings were observed by Taboada and Leece (2014) [17], Shinde *et al.* (2018) [16] Thejasree *et al.* (2018) [18] and Saikia *et al.* (2019) [14]. However non significant difference on respiratory rate in ketofol group was observed by. Decrease in respiration rate might be due to the respiratory depressant effect of ketamine and propofol both.

**Rectal temperature ($^0$C)**

In both group P and KP significant decrease ($P< 0.01$) in rectal temperature was observed from baseline (0 min) till 60 min. In group E non significant decrease in rectal temperature was observed from baseline (0 min) till 30 min but at 60 min the temperature insignificantly increased compared to 30 min.

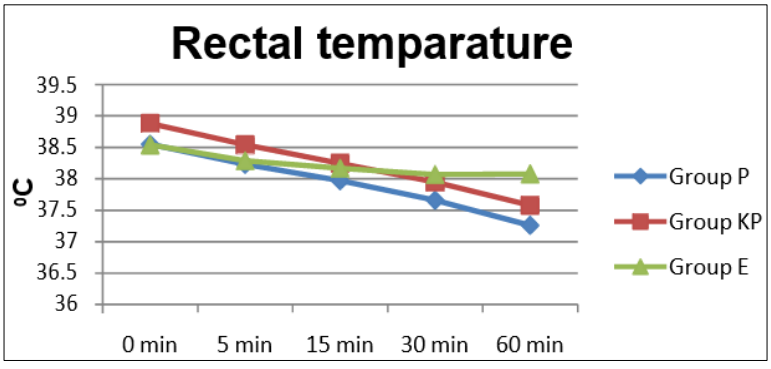


**Fig 3:** Rectal temperature (0C) at different time intervals in group P, KP and E

In group P significant decrease in rectal temperature was observed throughout the study period Thejasree *et al.* (2018) [18], Shinde *et al.* (2018) [16] and Saikia *et al.* (2019) [14] also observed decrease in propofol anaesthesia. In group KP rectal temperature was significantly decrease throughout the study period Thejasree *et al.*(2018) [18], Shinde *et al.* (2018) [16] and Saikia *et al.* (2019) [14]. In group E non significant decrease in rectal temperature was observed up to 30 min than at the end stage of study only a minimal increase on rectal temperature was observed. Hareesh *et al.* (2018) [6] and Perk *et al.* (2002) [10] observed decrease in temperature at the end of anaesthesia compared to baseline in etomidate anaesthesia. Decrease in temperature might be due to depression of thermoregulatory centre by anaesthetic drugs.

**Peripheral capillary oxygen saturation (SpO2) (%)**

In group P significant (P≤ 0.05) and group KP and E (P≤ 0.01) decrease in SpO2 was observed initially compared to baseline but at the end gradual increase in SpO2 towards baseline was observed although variations remain within normal physiological range im all groups. In group P significant decrease in SpO2 was observed due to effect of propofol Thejasree *et al.* (2018) [18] and Saikia *et al.* (2019) [14]. In group KP significant greater decrease in SpO2 was observed at 5 min but after that it increased towards the baseline. Similar finding was observed by Saikia *et al.* (2019) [14]. In group E significant decrease in SpO2 was observed at 5 min but after that it increased towards the baseline. Similar significant decrease in SpO2 was observed by Hareesh *et al.* (2018) [6] with etomidate. However all the SpO2 values remained within the normal physiological range (90-100%) in the present study.

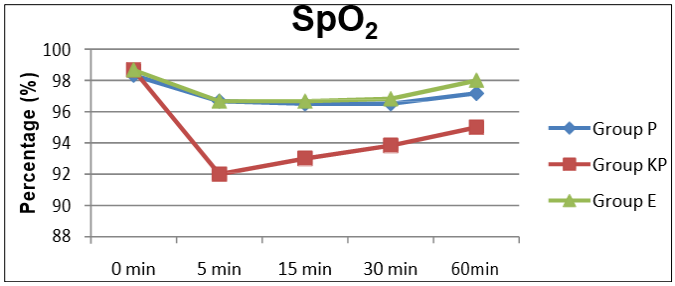


**Fig 4:** SpO2 (%) at different time intervals in group P, KP and E

**End-tidal carbon dioxide concentration (ETCO2) (mmHg)**

Insignificant increase (P≥ 0.05) ETCO2 value was observed at 5 min in all the groups and thereafter slight variations observed from 15 to 60 min time intervals in the groups. Among the groups at different time intervals no significant difference was recorded in the value of End-tidal carbon dioxide concentration (ETCO2).

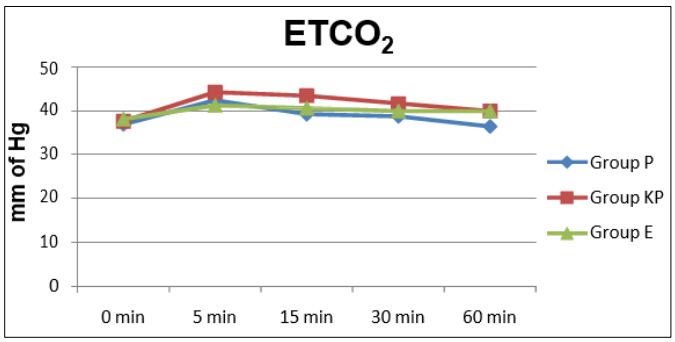


**Fig 5:** ETCO2 (mmHg) at different time intervals in group P, KP and E

In the present study non significant variation in ETCO2 value was observed within in the groups and among the groups at different time intervals. In group P non significant increase in ETCO2 was observed at 5 min after administration of propofol, and then gradually decreases towards the baseline. Similarly Mandsager *et al.* (2000) [9] reported non-significant change in ETCO2 with propofol anaesthetized dogs. Similarly non significant increase in ETCO2 followed by gradual decrease was observed with propofol anaesthesia in dogs by Sams *et al.* (2008) [15]. In group KP non significant increase in ETCO2 was observed at 5 min after administration of ketofol, and then gradually decreases towards the baseline. Similarly Daabiss *et al.* (2009) [4] recorded non significant changes in ETCO2 values after administering ketofol in human. In group E non significant increase in ETCO2 was observed at 5 min after administration of etomidate, and then gradually decreases towards the baseline. Similarly non significant changes were observed by Mandsager *et al.* (2000) [9] with etomidate anaesthesia in dogs. In another study non significantly higher ETCO2 values were observed at different time intervals in etomidate group compared propofol group in dogs by Sams *et al.* (2008) [15]. However non significant decrease in ETCO2 values was observed by Rodriguez *et al.* (2012) [13] which was contrary to the present findings.

**Systolic pressure (SP) (mmHg)**

In group P significant (*P*< 0.01) decrease in systolic pressure was observed up to 15 min time interval where as significantly (*P*< 0.01) increased SP up to 15 min in group KP followed by gradual decrease towards the baseline at the end of study period was observed. In group E systolic pressure showed non significant (P≥ 0.05) changes throughout the study period. Among the groups SP at 0 min did not show any significance difference but from 5 min to 60 min significant difference (*P*< 0.01) was observed among the group.

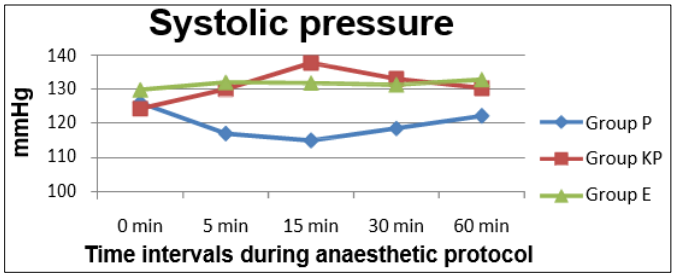


**Fig 6:** Systolic pressure (mmHg) of different time intervals in group P, KP and E

In group- P, decrease in SP initially might be due to effect of propofol. Similarly decrease in SP was observed by Brussel *et al.* (1989), Sams *et al.* (2008) [15], Amengual *et al.* (2013) [1] and Saikia *et al.* (2019) [14]. Increase in SP with ketofol anaesthesia was observed by Rao *et al.* (2015) and Saikia *et al.* (2019) [14] which might be due to the effect of ketamine present in ketofol combination. In group- E, SP remains constant till the end of study period. Similar findings observed by Sams *et al.* (2008) [15] and Rodriguez *et al.* (2012) [13].

**Diastolic pressure (DP) (mmHg)**

In group P significant (*P*< 0.01) decrease in diastolic pressure was observed up to 30 min time interval. However DP increased significantly (*P*≤ 0.01) up to 15 min followed by gradual decrease towards the baseline at the end of study period in group KP. In group E diastolic pressure showed non significant (P≥ 0.05) changes till the end of study period. In all the three groups (Group-P, Group-KP and Group-E), the mean value of diastolic pressure recorded at baseline (0 min) and 5 min did not show any significance difference but from 15 min to 60 min significantly (P≤ 0.01) low value of diastolic pressure was observed in group P compared to group KP and E.

In group- P, decreased Decrease in DP with propofol induction had also been reported by Brussel *et al.* (1989), Sams *et al.* (2008) [15], Amengual *et al.* (2013) [1], Taboada and Leece (2014) [17] and Saikia *et al.* (2019) [14] which might be because propofol causes a transient decrease in blood pressure (SBP, DBP and MAP) mainly due to peripheral vasodilation, decreased sympathetic outflow and myocardial

depression. In group- KP, the diastolic pressure increased significantly ($P< 0.01$) after induction. Increase in DP with ketofol anaesthesia was observed by Kumar *et al.* (2014) [8], Rao *et al.* (2015) [11], Cima *et al.* (2016) [3] and Saikia *et al.* (2019) [14] which might be due positive synergistic effect of propofol and ketamine when combined together (Larisa *et al.* 2010). In group- E, the diastolic pressure increased non significantly after induction with etomidate and then during maintenance of anaesthesia its remain stable till the end of anaesthesia. Similar findings observed by Sams *et al.* (2008) [15] and Rodriguez *et al.* (2012) [13]. There was significant difference ($P< 0.01$) of diastolic pressure (DP) among the three groups till end of experiment after induction. Significantly higher ($P< 0.01$) diastolic pressure was observed in group KP compared to group P and group E which might be due to different pharmacodynamic actions of different induction agents on cardiovascular system.

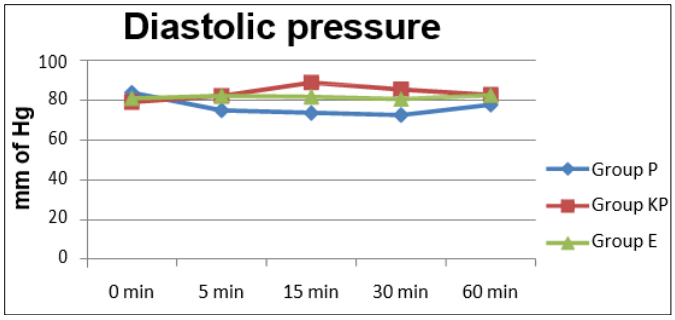


**Fig 7:** Diastolic pressure (mmHg) of different time intervals in group P, KP and E

## Conclusion

The heart rate initially increased and then decreased gradually towards pre-anaesthetic level in all the three groups. The respiratory rate initially decreased and then increased towards pre-anaesthetic level in all the three groups. Rectal temperature decreased in all three groups compared to baseline at the end of anaesthesia. SpO2 initially decreased in all three groups but towards the end it again increased towards the baseline. ETCO2 initially increased in all three groups but later on it decreased gradually towards pre-anaesthetic level in all the three groups. Both diastolic pressure and systolic pressure remained in a comfortable zone in group-E animals whereas, high SP and DP were recorded in group- KP animals and low blood pressure was recorded in group-P animals.

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